CLAIMS

1. A purified polynucleotide which encodes a polypeptide that inhibits the NF-κB signaling pathway, said polynucleotide being selected in the group consisting of:

(a) a polynucleotide which encodes a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39;

(b) a purified polynucleotide complementary to the one as defined in (a);

(c) a purified polynucleotide which is at least 70% identical to the polynucleotide as defined in (a);

(d) a purified polynucleotide which is at least 80% identical to the polynucleotide as defined in (a);

(e) a purified polynucleotide which is at least 90% identical to the polynucleotide as defined in (a) and

(f) a purified polynucleotide which hybridizes under stringent conditions to the polynucleotide as defined in (a), wherein said stringent conditions comprise washing in 5X SSC at a temperature from 50 to 68°C.

2. The purified polynucleotide of Claim 1, wherein said polypeptide inhibits the NF-κB pathway.

3. The purified polynucleotide of Claim 2, wherein said polypeptide disrupts NEMO oligomerization.

4. A vector comprising the purified polynucleotide of Claim 1.

5. A host cell comprising the purified polynucleotide of Claim 1.

6. A purified polypeptide that inhibits the NF-κB pathway selected in the group consisting of:

a) a NEMO type polypeptide having an amino acid sequence selected in the group consisting of SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33,

SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39;

b) a purified polypeptide which is at least 70% identical to the polypeptide as defined in a);

c) a purified polypeptide which is at least 80% identical to the polypeptide as defined in a);

(d) a purified polypeptide which is at least 90% identical to the polypeptide as defined in a);

(e) a purified polypeptide which is at least 95% identical to the polypeptide as defined in a).

7. The purified polypeptide of Claim 6, wherein said polypeptide inhibits the NF-κB pathway.

8. The purified polypeptide of Claim 7, wherein said polypeptide disrupts NEMO oligomerization.

9. A polypeptide fusion construct that inhibits the NF-κB pathway, said construct comprising an amino acid sequence being selected in the group consisting of:

a) a polypeptide fusion construct comprising an amino acid sequence selected in the group consisting of SEQ ID NO: 3, SEQ ID NO:7, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39 and which is linked to a polypeptide having a high transduction potential;

b) a polypeptide fusion construct comprising an amino acid sequence at least 80% identical to an amino acid sequence as defined in a);

c) a polypeptide fusion construct comprising an amino acid sequence at least 90% identical to an amino acid sequence as defined in a);

d) a polypeptide fusion construct comprising an amino acid sequence at least 95% identical to an amino acid sequence as defined in a);

e) a polypeptide fusion construct comprising an amino acid sequence that is at least 70% identical to an amino acid sequence selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 7, SEQ ID NO: 14, SEQ ID NO: 16, SEQ

ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39; said amino acid sequence being linked to a polypeptide having a high transduction potential.

10. The polypeptide of Claim 9, wherein said polypeptide fusion construct disrupts NEMO oligomerization.

11. The polypeptide of Claim 9, wherein said linked is by an amino acid spacer sequence having a length ranging from 1-35 amino acids.

12. The polypeptide of Claim 11, wherein said amino acid spacer sequence is selected from the group consisting of SEQ ID NO: 9 and SEQ ID NO: 10.

13. The polypeptide of Claim 9, wherein said polypeptide having a high transduction potential has an amino acid sequence of SEQ ID NO: 1.

14. The polypeptide of Claim 13, wherein the polypeptide fusion construct has the amino acid sequence selected in the group consisting of SEQ ID NO: 2, SEQ ID NO: 6, SEQ ID NO:13 and SEQ ID NO:15.

15. A method of inhibiting the NF-κB signaling pathway comprising contacting *in vitro* an eukaryotic cell with a polypeptide fusion construct of Claims 9 to 14.

16. A method of disrupting NEMO oligomerization comprising contacting *in vitro* said NEMO with a polypeptide fusion construct of Claims 9 to 14.

17. Use of an effective amount of a composition comprising a polypeptide fusion construct of Claims 9 to 14 and one or more pharmaceutically acceptable carriers or excipients, for the preparation of a medicament for modulating or treating a disorder regulated by the NF-κB signaling pathway in a subject in need thereof.

18. The use of Claim 17, wherein said subject in need thereof is a human.

19. The use of Claims 17 or 18, wherein said effective amount ranges from 0.1 mg/Kg/day to 30 mg/Kg/day.

20. The use of Claims 17 to 19, wherein said disorder regulated by the NF-κB signaling pathway is selected from the group consisting of inflammatory responses, oncogenesis, and viral infection.

21. The use of Claims 17 to 20, wherein said composition is administered in a form selected from the group consisting of oral, rectal, nasal, parenteral, intracisternal, intravaginal, intraperitoneal, sublingual, topical, and bucal administration.

22. The use of Claims 17 to 21, wherein said composition is administered preferably intravenously.

23. Use of an effective amount of a composition comprising a polypeptide fusion construct of Claims 9 to 14 and one or more pharmaceutically acceptable carriers or excipients, for the preparation of a medicament for regulating cell proliferation or apoptosis in a subject in need thereof.

24. The use of Claim 23, wherein said subject in need thereof is a human.

25. The use of Claim 23 or Claim 24, wherein said effective amount ranges from 0.1 mg/Kg/day to 30 mg/Kg/day.

26. The use of Claims 23 to 25, wherein said composition is administered in a form selected from the group consisting of oral, rectal, nasal, parenteral, intracisternal, intravaginal, intraperitoneal, sublingual, topical, and bucal administration.

27. The use of Claims 23 to 26, wherein said composition is administered preferably intravenously.

28. Use of an effective amount of a composition comprising a polypeptide fusion construct of Claims 9 to 14 and one or more pharmaceutically acceptable carriers or excipients, for the preparation of a medicament for regulating B or T lymphocytes in antigenic stimulation in a subject in need thereof.

29. The use of Claim 28, wherein said subject in need thereof is a human.

30. The use of Claim 28 or Claim 29, wherein said effective amount ranges from 0.1 mg/Kg/day to 30 mg/Kg/day.

31. The use of Claims 28 to 30, wherein said composition is administered in a form selected from the group consisting of oral, rectal, nasal, parenteral, intracisternal, intravaginal, intraperitoneal, sublingual, topical, and bucal administration.

32. The use of Claims 28 to 31, wherein said composition is administered preferably intravenously.

33. A method of identifying polypeptides that modulate oligomerization of NEMO comprising:

a) identifying a candidate polypeptide sequence;

b) creating a polypeptide fusion construct by linking said candidate polypeptide sequence to a polypeptide having a high transduction potential via a spacer sequence;

c) contacting a cell culture with the polypeptide fusion construct; and

d) monitoring the activity of the NF-κB signaling pathway;

e) comparing the activity of the NF-κB signaling pathway in the presence of said polypeptide fusion construct to the activity of the NF-κB signaling pathway in the absence of said polypeptide fusion construct to determine the relative inhibition by said polypeptide fusion construct; and

f) correlating relative inhibition by said polypeptide fusion construct to NEMO oligomerization.

34. The method of Claim 33, wherein said candidate polypeptide sequence has a coiled-coil or helical structure.

35. The method of Claim 33 or Claim 34, wherein said candidate polypeptide sequence has 20-60 amino acids.

36. The method of Claims 33 to 35, wherein said candidate polypeptide sequence is derived from NEMO.

37. The method of Claims 33 to 36, wherein said spacer sequence has a length ranging from 1-35 amino acids.

38. The method of Claim 37, wherein said spacer sequence is selected from the group consisting of SEQ ID NO: 9 and SEQ ID NO: 10.

39. The method of Claim 33, wherein said polypeptide having a high transduction potential has an amino acid sequence of SEQ ID NO: 1.

40. The method of Claim 33, wherein said cell culture comprises pre-B 70Z/3 lymphocytes that have been transfected with NF-κB dependent β-glactosidase reporter gene, deposited at the CNCM (Collection Nationale de Cultures

de Microorganismes), 28 rue du Docteur Roux, 75724 PARIS Cedex 15, France, on April 1st, 2003 under number I-3004.

41. The method of Claim 33, wherein said polypeptide fusion construct further comprises an N-terminal cysteine residue.

42. The method of Claim 39, further comprising:

b-1) labeling said polypeptide fusion construct; and

c-1) monitoring cellular uptake of the labeled polypeptide fusion construct.

43. The method of Claim 42, wherein said labeling comprises chemically reacting the cysteine residue with a fluorophore.

44. The method of Claim 43, wherein said fluorophore is BODIPY.

45. The method of Claim 42, wherein said monitoring cellular uptake is by FACS.